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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,033	07/23/2001	Bettina Bommanus	210212US0X	2456
22850	7590	04/06/2004	EXAMINER	
OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			PAK, YONG D	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 04/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/910,033	<b>Applicant(s)</b> BOMMANUS ET AL.	
	<b>Examiner</b> Yong D Pak	<b>Art Unit</b> 1652	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 1/20/2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,8-12,19-25 and 32-35 is/are pending in the application.
- 4a) Of the above claim(s) 8-12,19-25 and 32-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

The amendment filed on January 20, 2004, amending claims 1 and 12, canceling claims 6, 17, 30 and 40, has been entered.

Claims 1, 8-12, 19-25 and 32-35 are pending.

### ***Election/Restrictions***

Claims 8-12, 19-25, 32-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

Notice of Possible Rejoinder: The Examiner notes that if claim 1 is found directed to an allowable product, then claim 12, which is directed to the process of making the patentable product, respectively, previously withdrawn from consideration as a result of a restriction requirement, would now be rejoined pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86; see also MPEP 821.04, *In re Ochiai*, and *In re Brouwer*). Since process claims 12 and 17 would be rejoined and fully examined for patentability under 37 CFR 1.104, applicants are instructed to amend said claims as deemed necessary according to rejections made against the elected claims.

### ***Claim Rejections - 35 USC § 103***

Art Unit: 1652

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hummel et al.

The mutant *Lactobacillus brevis* dehydrogenase of SEQ ID NO:2 of the instant invention differs from the wildtype dehydrogenase by one residue, an Aspartic acid at position 38 instead of a Glycine. Position 37 of the dehydrogenase of Hummel et al. is corresponds to position 38 of SEQ ID NO:2 because Hummel et al. is not including the initial Met residue. Therefore, position "38" will be used to refer to both positions of Hummel et al. and the instant invention.

Hummel et al. (WO 99/47684 – form PTO-1449) teach a mutant dehydrogenase comprising of a glycine at position 10, **aspartic acid at position 38**, a leucine at position 39 and a methionine residue at position 49. Hummel et al. teach that the mutant dehydrogenase has a greater affinity towards NAD(H) (pages 2-6 and 28-29).

Hummel et al. teach that the disadvantage of the use of an *L. kefir* or *L. brevis* alcohol dehydrogenase is that the enzymes require the co-enzyme NADP(H) and this co-enzyme is substantially less stable and more expensive than NAD(H) (page 1). Hummel et al. teach that decreasing the alkalinity of the dehydrogenase in the co-

Art Unit: 1652

enzyme docking area can increase the enzyme's preference for NAD(H) rather than for NADP(H) (abstract).

Hummel et al. teach that the basicity of amino acids in the coenzyme docking area can be reduced by displacement of **neutral** or positively charged amino acids with **negatively charged amino acids** (abstract and page 2, 2<sup>nd</sup> paragraph). Therefore, the disclosure of Hummel et al. is not solely drawn to modifying alcohol dehydrogenases by altering only basic amino acids, but also altering neutral amino acids with acidic amino acids or negatively charged amino acids to lower the basicity of the amino acids in the coenzyme docking area. This coenzyme docking area is specifically taught in the disclosure, page 2.

Hummel et al. does not teach a mutant an alcohol dehydrogenase consisting of an aspartic acid at position 38 of a *L. brevis* or *L. kefir* alcohol dehydrogenase.

However, it would have been obvious to one having ordinary skill in the art to apply the teachings of Hummel et al. and make mutants consisting of only one mutation selected from A10G, G38D, R39L or K49M. Hummel et al. teach that the binding location for the co-enzyme is in the area around position 38 and/or 39 (pages 28-29).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a mutant *L. brevis* alcohol dehydrogenase having an aspartic residue at position corresponding to 38. The motivation of making such a mutant is to decrease the alkalinity of the enzyme to increase its affinity towards NAD(H). One of ordinary skill in the art would also have been motivated to make such a mutant to determine whether the increase affinity

Art Unit: 1652

towards NAD(H) of the mutant of Hummel et al. is due to the synergistic effects of the four mutations or if one mutation is capable of increasing the enzyme's affinity towards NAD(H). One of ordinary skill in the art would have had a reasonable expectation of success since residue 38 lies in the co-enzyme docking area.

### ***Response to Arguments***

The rejections of claim 6 under 103(a) has been withdrawn in light of the cancellation of claim 6.

The rejections of claim 1 under 112, 2<sup>nd</sup> paragraph has been withdrawn in light of the amendment of claim 1.

The rejections of claim 1 under 102(b) has been withdrawn in light of the amendment of claim 1.

### ***Claim Rejections - 35 USC § 103***

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hummel et al. (WO 99/47684 – form PTO-1449)

Applicants argue that Hummel et al. do not teach a mutant *L. brevis* alcohol dehydrogenase having only one mutation, the Glycine residue at position 38, but a mutant comprising multiple mutations. The examiner disagrees.

The motivation of modifying position 38 is to decrease the alkalinity of the enzyme to increase its affinity towards NAD(H). Hummel et al. teach that decreasing

Art Unit: 1652

the alkalinity of the dehydrogenase in the co-enzyme docking area can increase the enzyme's preference for NAD(H) rather than for NADP(H) (abstract). The binding location for the co-enzyme is in the area around position 38 and/or 39 (pages 28-29).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a mutant *L. brevis* alcohol dehydrogenase having an aspartic residue at position corresponding to 38. One of ordinary skill in the art would also have been motivated to make such a mutant to determine whether the increase affinity towards NAD(H) of the mutant of Hummel et al. is due to the synergistic effects of the four mutations or if one mutation is capable of increasing the enzyme's affinity towards NAD(H). One of ordinary skill in the art would have had a reasonable expectation of success since residue 38 lies in the co-enzyme docking area.

No claim is allowed.

### **Conclusion**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

Art Unit: 1652

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak  
Patent Examiner



PONNATHAPU ACHUTAMURTHY  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER